UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader
January 15, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

May 21, 1998

MEMORANDUM

Subject: **Parathion (057501).** The outcome of the HED Metabolism Assessment Review Committee Meeting Held on March 11, 1998. DP Barcode: D245193

From: Bonnie Cropp-Kohlligian, Environmental Scientist
Reregistration Branch II
Health Effects Division [7509C]

Through: Alan P. Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division [7509C]

And

Alberto Protzel, Branch Senior Scientist
Toxicology Branch I
Health Effects Division [7509C]

And

Richard Loranger, Chair
Metabolism Assessment Review Committee
Health Effects Division [7509C]

To: George Kramer, Executive Secretary
Metabolism Assessment Review Committee
Health Effects Division [7509C]

Background

Parathion was previously discussed by the HED Metabolism Committee on 1/30/95. Available animal metabolism data were presented and discussed. Livestock feeding studies were not available. [Note: The Committee did not discuss parathion residues of concern in plant commodities.] The Committee concluded the following (memo by S. Hummel dated 2/10/95):

- It was postulated that deethylation of the phosphorodithioate or phosphorothioate would lower the toxicological activity. The electron donating properties of NH_2 substitution in

the para position on the phenyl ring produce a metabolite less toxic than parathion. Some evidence suggests that 4-acetamidoparaoxon may be less toxic than parathion, but in the absence of toxicology on that compound, it will be assumed to be as toxic as parent.

- The parathion residue to be regulated will include parathion, paraoxon, and 4-acetamidoparaoxon. *P*-Nitrophenol is not a residue of concern. If the registrant can demonstrate that 4-acetamidoparaoxon is much less toxic than parathion, feeding study data may not be needed for 4-acetamidoparaoxon. 4-Acetamidoparaoxon will not be considered a residue of concern if the acute oral LD_{50} is more than 200 mg/kg. If the acute oral LD_{50} is less than 200 mg/kg, additional toxicological testing may be required.

Current Considerations

In light of FQPA requirements to perform cumulative risk assessments and the associated issue of addressing common metabolites, previous conclusions reached by the HED Metabolism Committee on 1/30/95 concerning *p*-nitrophenol needed to be reconsidered since *p*-nitrophenol is also a metabolite of methyl parathion. Moreover, to insure consistency between methyl parathion and parathion, the HED Metabolism Assessment Review Committee* met on 3/11/98 to discuss both chemicals and determine what residues of parathion need to be regulated/included in the risk assessment from plant and animal commodities.

Available plant and animal metabolism data were presented and discussed. [NOTE: No new animal metabolism or animal magnitude of the residue data had been submitted since the previous meeting of the HED Metabolism Committee on 1/30/95.] The HED Chapter of the Paranitrophenol Reregistration Eligibility Decision (RED) document was briefly discussed. The Committee concluded the following:

- Based on available plant metabolism data, parathion residues of concern in/on plant commodities are parathion, paraoxon, and *p*-nitrophenol. Parathion residues of concern to be included in the risk assessment for plant commodities based on cholinesterase inhibition will include parathion and paraoxon. The tolerance expression may be based on parathion only since detectable levels of paraoxon have not been found in/on commodities tested by FDA monitoring. Residues of *p*-nitrophenol resulting from the use of parathion do not have to be included in the tolerance expression or considered in the aggregate risk assessment for parathion with respect to cholinesterase inhibition, but should be considered in conjunction with the cumulative risk assessment for *p*-nitrophenol. The risk assessment for *p*-nitrophenol will be based on its own toxicological endpoints (rather than cholinesterase inhibition) and should include exposure to *p*-nitrophenol from its use as a fungicide on leather. Residues of parathion, paraoxon, and *p*-nitrophenol should be determined in/on plant samples collected from future plant magnitude of the residue studies.

- Based on available animal metabolism data, parathion residues of concern in animal commodities are parathion, paraoxon, *p*-nitrophenol, and 4-acetamidoparaoxon. [Note: Livestock feeding studies remain outstanding.] Parathion residues of concern to be included in the risk assessment for animal commodities based on cholinesterase inhibition will include parathion, paraoxon, and 4-acetamidoparaoxon. As with plants, the tolerance expression may be based on parathion only. Residues of *p*-nitrophenol do not have to be included in the tolerance expression or considered in the aggregate risk assessment for parathion but should be considered in conjunction with the cumulative risk assessment for *p*-nitrophenol. The risk assessment for *p*-nitrophenol will be based on its own toxicological endpoints (rather than cholinesterase inhibition) and should include exposure to *p*-nitrophenol from its use as a fungicide on leather. Residues of parathion, paraoxon, *p*-nitrophenol, and 4-acetamidoparaoxon should be determined in meat, milk, poultry, and egg tissue samples from the required livestock feeding studies.

  NOTE: Toxicology deems 4-acetamidoparaoxon of concern due to potential cholinesterase inhibition. However, if the registrant can demonstrate that 4-acetamidoparaoxon is much less toxic than parathion, feeding study data will not be needed for 4-acetamidoparaoxon and 4-acetamidoparaoxon residues in animal commodities will not need to be included in the risk assessment for parathion. 4-Acetamidoparaoxon will not be considered a residue of concern if the acute oral LD_{50} is more than 200 mg/kg. If the acute oral LD_{50} is less than 200 mg/kg, additional toxicological testing may be required.

- For the aggregate risk assessment for parathion with respect to cholinesterase inhibition, the residues of concern in drinking water are parathion and paraoxon. Residues of *p*-nitrophenol in drinking water should be included in the cumulative risk assessment for *p*-nitrophenol.

* Committee Members in Attendance:

R. Loranger
C. Olinger
G. Kramer
A. Protzel
L. Cheng
K. Farwell
J. Peggins

cc: HED Metabolism Assessment Review Committee file (G. Kramer), BLCKohlligian, Parathion Reg. Std. File, Parathion SF, RF.

7509C:RRB2:BLCKohlligian:CM#2:Rm 804E:703-305-7462:4/10/98.